

REMARKS

1. The Claims

Claims 1 – 12 were previously canceled. Claims 13-26 were pending in this application. Claims 17-24 have been withdrawn as being drawn to a non-elected invention. Claims 13-16 and 25-26 stand rejected in this application.

In the claims listing above, claims 13-16 and 26 are amended, and claims 27-30 are newly added. Therefore, upon entry of the amendments to the claims, claims 13-16 and 25-30 will be pending.

New dependent claims 27-30 recite methods of treatment of neuralgia pain or neuropathic pain that is accompanied by an increase in muscle tone. Support for these claims can be found in the originally filed claims and in the specification in Paragraph [0010].

2. The Amendments to the Specification

The title has been amended to replace “Pains” with its singular form “Pain.”

3. Claim rejections under 35 USC 112

Claims 13-16 and 25-26 are rejected under 35 USC §112, second paragraph, as being indefinite. Examiner contends that the recitation “neuralgia pain, also known as neuropathic pain” in claim 13 recites a broad limitation followed by a narrower range/limitation. Claim 13 is amended from “neuralgia pain, also known as neuropathic pain” to “neuralgia pain or neuropathic pain” to obviate this rejection.

Similarly, the Examiner contends that the recitation “tolperisone or its analogs, such as eperisone or silperisone” in claim 16 also recites a broad limitation followed by a narrower range/limitation. Claim 16 is amended from “tolperisone or its analogs, such as eperisone or silperisone” to “tolperisone, eperisone, silperisone” to obviate this rejection.

Claims 14 and 16 are also rejected under 35 USC §112, second paragraph. Examiner contends that the recitation of “tolperisone or an analog thereof” is indefinite because it is not clear

what the term “an analog thereof” refers to. By the deletion of the expression “or its analogs” from claim 16, this rejection of claim 16 is now moot. With respect to claim 14, Applicants respectfully traverse because it is readily apparent to one of skill in the art what the term “tolperisone analog” refers to. *See, e.g.*, U.S. Pat. No. 4,181,803 “Propiophenone Derivatives in the Treatment of Pathological Muscular Conditions” to Morita et al. (Cols. 1-2); U.S. Pat. No. 4,528,299 “1-(2,3-Dimethyl-4-Methoxyphenyl)-2-Methyl-3-(1-Pyrrolidinyl)-1-Propanone and Anti-spastic use thereof” to Uno et al (Cols. 3-4, Table 1).

Claims 13-14, 16 and 25-26 are rejected under 35 USC §112, second paragraph as allegedly failing to enable a person skilled in the relevant art to practice the invention commensurate in scope with those claims. The Examiner has acknowledged that the specification is enabling for specific sodium channel inhibitors, but the Examiner asserts that the specification is not enabling for “sodium channel inhibiting or-influencing substance[s].” Applicants respectfully traverse, but in order to expedite prosecution, Applicants have amended claim 13 by adding the limitation that the “sodium channel inhibiting or-influencing substance” must be “selected from the group consisting of tolperisone, eperisone, silperisone, and other tolperisone analogs, and riluzole, propafenone, lidocaine, flecainide and metixen, and their pharmaceutically utilizable salts.” In view of the narrower breadth of the amended claims, Applicants respectfully submit that the amended claims are allowable.

4. Claim rejections under 35 USC 103(a)

Claims 12-15 and 23-25 stand rejected under 35 USC §103(a) in view of Lobisch et al. (US 5,162,346) over Cai et al. (US 6,281,211). In order to establish a *prima facie* case of obviousness there must be some suggestion or motivation in the prior art to combine reference teachings. MPEP §2143. There is no suggestion in the cited prior art for the combination of flupirtine with the sodium channel blockers in claim 1. Because neither reference expressly suggests the combination use of flupirtine with a sodium channel blocker for the treatment of neuropathic pain, it appears that the Examiner is relying on a combination of equivalents known for the same purpose to establish a *prima facie* case of obviousness. MPEP §2144.06. Potassium channel openers and sodium channel blockers are not equivalent substances. Potassium channel openers and sodium channel blockers

are each distinct art recognized classes of materials, and are not considered equivalents in the relevant art.

Furthermore, Cai teaches away from a combination of sodium channel blockers and potassium channel openers for neuropathic pain. Discussing the uses of sodium channel inhibitors, Cai writes that “[i]n addition to the above-mentioned clinical uses, [three of the previously mentioned sodium channel blockers] are *occasionally* used to treat neuropathic pain.” Column 1, lines 49-54 (emphasis added). Cai implies that the use of sodium channel blockers to treat neuropathic pain is unusual; and hence one of skill in the art would not be motivated to combine the use of sodium channel blockers with another class of compounds to treat neuropathic pain. Consequently, Applicants respectfully submit that a *prima facie* case of obviousness has not been established and therefore a rejection of the claims on this basis would be improper.

Even if a *prima facie* case of obviousness were established, it would be rebutted by unexpected results for combinations of flupirtine with a sodium channel inhibitor, in this case tolperisone. In the specification, in the section titled “PHARMACOLOGICAL EXAMPLES,” Applicants show that there is a synergistic muscle-relaxing effect of combinations of flupirtine and tolperisone in both rats and mice. *See* Tables 1, 2, 3, 4 (showing that the measured muscle relaxation is significantly higher than that calculated assuming no synergy). Furthermore, while Applicants show that the desirable muscle-relaxing effect is synergistic, Applicants show that the undesirable effect on motor coordination is merely additive. *See* Tables 5 & 6 (showing that the effect on muscle coordination is what would be expected assuming no synergy). Therefore, Applicants respectfully submit that a rejection of these claims for obviousness would be improper.

Claims 14 and 16 also stand rejected under 35 USC §103(a) in view of Lobisch over Cai, and further in view of the applicants admitted prior art of record in the specification. For the same reasons discussed above regarding the nonobviousness of Lobisch over Cai, Applicants respectfully submit that a rejection of these claims for obviousness would be improper.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the claim rejections and respectfully submit that this application is now in condition for allowance, which action is earnestly solicited. If any issues remain that could be addressed by a telephone conversation, the Examiner is cordially invited to contact Applicants' undersigned attorney at the number shown below.

Respectfully submitted,

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